

FDA approval of new formulation of Kaletra

Today (October 28, 2005) the Food and Drug Administration approved a new formulation of Kaletra. Kaletra (lopinavir/ritonavir) is now available as a film coated tablet (200mg/50mg) that provides advantages over the currently marketed capsule formulation for HIV-1 infected patients. Specifically, the tablet formulation:

- does not require refrigeration,
- can be administered without regard to meals
- does not require dose adjustments for concomitant use with certain NNRTIs and PIs in treatment-naïve patients
- has a decreased pill burden compared to the capsule formulation (2 tablets twice daily or 4 tablets once daily in treatment-naïve patients only vs 3 capsules twice daily or 6 capsules once daily in treatment-naïve patients only)

The following additions and revisions were made to the package insert.

1. The CLINICAL PHARMACOLOGY section contains the following additions:

Pharmacokinetics

Plasma concentrations of lopinavir and ritonavir after administration of two 200/50 mg KALETRA tablets are similar to three 133.3/33.3 mg KALETRA capsules under fed conditions with less pharmacokinetic variability.

Effects of Food on Oral Absorption

KALETRA tablets

No clinically significant changes in C_{max} and AUC were observed following administration of Kaletra tablets under fed conditions compared to fasted conditions. Relative to fasting, administration of KALETRA tablets with a moderate fat meal (500 – 682 Kcal, 23 to 25% calories from fat) increased lopinavir AUC and C_{max} by 26.9% and 17.6%, respectively. Relative to fasting, administration of KALETRA tablets with a high fat meal (872 Kcal, 56% from fat) increased lopinavir AUC by 18.9%, but not C_{max} . Therefore, Kaletra tablets may be taken with or without food.

Drug-drug Interactions

Tables 2 and 3 were updated to clarify which formulations of Kaletra (capsule, oral solution or tablets) were used in the drug-drug interaction studies. Results of the drug-drug interaction study between efavirenz and Kaletra tablets were included.

2. The following text was added and/or revised in the PRECAUTION: Information for patients section:
- KALETRA tablets can be taken at the same time as didanosine without food. Patients taking didanosine should take didanosine one hour before or two hours after KALETRA oral solution.
 - KALETRA tablets may be taken with or without food. KALETRA oral solution should be taken with food to enhance absorption.
3. In the PRECAUTION section, Table 10: Established and Other Potentially Significant Drug Interactions, was revised to include the following:
- KALETRA tablets can be taken at the same time as didanosine without food.
 - The saquinavir dose is 1000 mg BID when co-administered with Kaletra 400/100 mg BID.
4. The DOSAGE AND ADMINISTRATION section was revised to include the following information regarding the new tablet formulation:
- KALETRA tablets may be taken with or without food.
 - KALETRA oral solution must be taken with food.
 - KALETRA tablets should be swallowed whole and not chewed, broken, or crushed.

The recommended oral dose of KALETRA is as follows: (Please refer also to **INDICATIONS AND USAGE** and **ADVERSE REACTIONS**)

Adults

Therapy-Naïve Patients

- KALETRA tablets 400/100 mg (2 tablets) twice-daily with or without food.
- KALETRA oral solution 400/100 mg (5.0 mL) twice-daily taken with food.
- KALETRA tablets 800/200 mg (4 tablets) once-daily taken with or without food.
- KALETRA oral solution 800/200 mg (10 mL) once-daily taken with food.

Therapy-Experienced Patients

- KALETRA tablets 400/100 mg (2 tablets) twice-daily taken with or without food.
- KALETRA oral solution 400/100 mg (5.0 mL) twice-daily taken with food.

Once-daily administration of KALETRA is not recommended in therapy-experienced patients.

Concomitant therapy: Efavirenz, nevirapine, fosamprenavir or nelfinavir

- KALETRA 400/100 mg tablets can be used twice-daily in combination with these drugs with no dose adjustment in antiretroviral-naïve patients.
- A dose increase of KALETRA tablets to 600/150 mg (3 tablets) twice-daily may be considered when used in combination with efavirenz, nevirapine, fosamprenavir without ritonavir, or nelfinavir in treatment-experienced patients where decreased susceptibility to lopinavir is clinically suspected (by treatment history or laboratory evidence).
- A dose increase of KALETRA oral solution to 533/133 mg (6.5 mL) twice-daily taken with food is recommended when used in combination with efavirenz, nevirapine, amprenavir or nelfinavir.

Increasing the dose of KALETRA tablets to 600/150 mg (3 tablets) twice-daily coadministered with efavirenz significantly increased the lopinavir plasma concentrations approximately 35% and ritonavir concentrations approximately 56% to 92% compared to KALETRA tablets 400/100 mg twice-daily without efavirenz (see **CLINICAL PHARMACOLOGY– Drug-drug Interactions Table 2 and/or PRECAUTIONS – Table 10**).

KALETRA tablets and oral solution should not be administered as a once-daily regimen in combination with efavirenz, nevirapine, amprenavir or nelfinavir.

5. The HOW SUPPLIED section was revised to include storage information for the Kaletra tablets as follows:
Recommended storage: Store KALETRA film-coated tablets at 20°- 25°C (68°-77°F); excursions permitted to 15°-30°C (59° to 86°F) [see USP controlled room temperature]. Dispense in original container. For patient use: exposure of this product to high humidity outside the original container for longer than 2 weeks is not recommended.

The capsule formulation will be phased out over time by the company.

Kaletra is a product of Abbott Laboratories. The original formulation was approved on September 15, 2000.

Richard Klein
Office of Special Health Issues
Food and Drug Administration

Kimberly Struble
Division of Antiviral Drug Products
Food and Drug Administration

An archive of past list serve announcements is available on the FDA web site at <http://www.fda.gov/oashi/aids/listserv/archive.html>

This release was provided by the FDA and posted on
AIDSinfo Web site (<http://AIDSinfo.nih.gov>).